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THE ROLE OF CALCIUM IN OSTEOPOROSIS

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INTRODUCTION

Osteoporosis is a complex disorder of multifactorial origin that is characterized by an asymptomatic reduction in the quantity of bone mass per unit volume (4). When bone mass becomes too low, structural integrity and mechanical support are not maintained, and fractures occur with minimal trauma. The most common sites of osteoporotic fracture are the proximal femur, distal radius, vertebra, humerus, pelvis, and ribs. In clinical research, such a diagnosis is frequently applied only to patients with one or more fractures (76) even though it may be detected in many patients by measuring

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bone mass with single or dual photon absorptiometry (SPA or DPA) (71) or with quantitative computerized tomography (QCT) (32).

Osteoporosis occurs most frequently in postmenopausal white women and in the elderly (14). About 20% of women suffer osteoporotic fractures by age 65, and more than 30% sustain fractures by age 90 (65). Significant osteoporosis is not observed in men and black women until after age 60, when fracture rates progressively increase.

BONE AND MINERAL METABOLISM

Bone is composed primarily of calcium and phosphorus in the form of hydroxyapatite crystals deposited in a collagen matrix (121). There are two types of bone in adults, cortical and trabecular (4). Cortical bone provides rigidity and is the major component of tubular bones (appendicular skeleton). Trabecular bone is spongy in appearance, provides strength and elasticity and constitutes about 60 to 70% of the vertebrae (axial skeleton).

Bone is a metabolically active tissue that turns over constantly. This process is regulated by cellular activities that resorb (osteoclastic) and form (osteoblastic) bone. In normal adult bone, resorption is coupled to and exactly balanced by formation so that no net change in the amount of bone is produced (26). To either increase or decrease net bone mass, these cellular processes must become functionally uncoupled, an event that is poorly understood at this time. By contrast, the major mineral ions of bone (calcium, phosphorus and magnesium) play a more passive role in bone mass changes. They must be present at physiologic concentrations in extracellular fluids for normal bone mineralization (formation) to occur (67). Dietary minerals help to maintain extracellular concentrations by replacing minerals lost to obligatory processes (urine, stool, and sweat) or those normally distributed to bone and soft tissues (35).

Maximum bone mass is achieved by about age 25–30 years, is maintained without much change until 35–45 years, and is lost at a constant rate of 0.3–0.5% per year in both men and women thereafter (35, 64, 90). For about 8–10 years immediately prior to and after menopause, most Caucasian women lose bone at a rate of 2–5% per year.

ASSOCIATION OF DIETARY FACTORS WITH OSTEOPOROSIS

Epidemiologic and Clinical Studies

CALCIUM

Absorption and balance Calcium balance generally reflects the degree of coupling of bone formation and resorption processes. Negative balances are

recorded when resorption exceeds formation and positive balances when formation exceeds resorption. It is important to recognize that because 99% of body calcium is in bone, it is not possible to build bone without positive calcium balance nor to be in negative balance without losing bone.

Knowing the amount of dietary calcium needed to achieve "zero balance" is key to setting nutritional requirements for calcium. However, the metabolic balance technique used to determine calcium balance has important theoretical and practical limitations that can result in inaccuracies. Calcium balance depends upon a number of factors including the amount of calcium in the diet, the efficacy of calcium absorption by the intestine, and excretion of calcium. Intestinal absorption of calcium decreases with age (28, 39, 46), which may be due to an age-related decrease in serum levels of 1,25-dihydroxyvitamin D [1,25(OH)2D3] (120), the biologically active metabolite of vitamin D that is produced by the kidney and regulates intestinal calcium absorption (17, 85). Serum immunoreactive and bioactive parathyroid hormone (25) increase with age, which is probably a response to the age-associated decrease in calcium absorption and probably represents secondary hyperparathyroidism. It is unknown whether this endocrine adaptive response to decreased calcium absorption contributes to the decreased skeletal mass and increased incidence of fractures seen in the elderly.

Relationship between calcium intake and bone mass, osteoporosis, and fracture There are two major methodologic problems in evaluating the evidence relating calcium intake to bone mass. One is the inaccuracies inherent in determining dietary calcium by historical recall and the relation of that data to lifetime intake. Another is the inconstant use of different methods to measure bone mass; some measure predominantly cortical bone and others trabecular bone. Furthermore, methods to identify altered geometric and structural properties, so far not available, may be important to identify osteoporotic bone accurately (34, 36).

Decreased skeletal mass is the most important risk factor for bone fracture without significant trauma (35, 104). The level of bone mass achieved at skeletal maturity (peak bone mass) is a major factor modifying the risk of development of osteoporosis. The more bone mass available before age-related bone loss, the less likely it will decrease to a level at which fracture will occur (35, 90). Another major factor modifying osteoporosis risk is the rate of bone loss as life progresses.

Normally, longitudinal bone growth is complete sometime during the second decade of life. For this to occur normally, positive calcium balance is needed in the range of 110 mg/day for females and 140 mg/day for males. During the adolescent growth spurt, the required calcium retention is two to three times higher (30, 84), and the Food and Nutrition Board (76a) recommends intakes of 1200 mg/day for those 10 to 19 years of age.

Opinion is mixed as to the age at which peak bone mass is achieved. Data concerning this issue is available only from studies using cross-sectional designs (1, 30, 70, 118). They show that bone mass does not appear to reach maximum levels until sometime during the mid twenties or early thirties, or 5 to 10 years after longitudinal bone growth has ceased. It is thought that during this period cortical porosity, increased during the adolescent growth spurt, is filled in and bone cortices become thicker. The quantity of bone mass that can be added is unclear, but it is estimated to be 5–10% (90). The optimum calcium retention to achieve this apparent increment in bone mass is not yet known but is probably in the range of 40 to 60 mg/day (70). The Food and Nutrition Board incorporated this view into the latest Recommended Dietary Allowances (76a) and extended the period during which positive calcium balance must be maintained to achieve peak bone mass. Thus, the RDA for the age group 20–25 years is the same as for 10–19 years or 1200 mg/day.

Many published reports have shown either no (3, 30, 52, 56, 89, 106, 113, 114, 118) or only a modest positive relationship between bone mass and dietary calcium (especially lifetime intake) (11, 16, 31, 33, 50, 70, 92).

Nordin (83) reported the results of an international investigation of calcium intake and osteoporotic fractures. In spite of inconsistent methods in the reporting of calcium intakes by the countries involved, it was possible to demonstrate an inverse rank order relation between calcium intakes and osteoporotic vertebral fracture frequency (determined by spine X-ray). Japanese women, whose calcium intake averaged 400 mg/day, had the highest frequency of fracture, and Finland, with the highest intake (1300 mg/day), had the lowest fracture frequency. This relationship did not hold for some countries. Whereas calcium intakes in Gambia and Jamaica were low, osteoporotic fractures were rare. Recently, Holbrook et al (43) related calcium intake data collected in 1973 to subsequent hip fracture incidence among 957 Caucasian adults (50–79 years in 1973). The group suffering hip fracture had a lower nutrient density of calcium than the group without fracture. The most widely cited of the papers showing a positive effect of calcium is that of Matkovic et al (70) which reported a 5–10% greater metacarpal cortical volume in the inhabitants of a Yugoslavian district with a high calcium intake as compared with the inhabitants of a district with a low calcium intake. The inhabitants of the "high calcium" district also had a 50% lower incidence of hip fractures. In contrast, no difference was detected in the incidence of fractures about the wrist. Because the differences in bone mass as a function of age were constant, it is likely that high lifelong intakes of calcium in the high calcium district increased peak cortical bone mass rather than prevented bone loss. In contrast to these results, Riggs et al (106) found no relationship

between the calcium intakes (range 260 to 2003 mg/day, mean 922 mg/day) of 106 normal women, age 23 to 84 years, and the rates of change in bone mineral density at the midradius (determined by single photon absorptiometry, SPA) and the lumbar spine (determined by dual photon absorptiometry, DPA) over a mean period of 4.1 years.

Most clinical studies of dietary calcium in osteoporotic patients show lower intakes than in age-matched control subjects (62, 82, 103). Whereas dietary calcium was lower than 800 mg/day in both patients and controls in all of these investigations, intakes were greater than 800 mg/day in a study in which no differences in calcium intake between osteoporotic patients and controls were demonstrated (84). The results of this latter study support Heaney's view (35) that low dietary calcium may play a permissive rather than a causative role in the development of osteoporosis and that this role can be demonstrated best when dietary calcium is below a "saturation" level.

Effects of calcium supplementation on bone mass and fracture The long-term effects of calcium supplementation on bone mass are not yet established. The results of investigations over two years or less are mixed. In general, they show a slowing of bone loss measured at sites comprised mostly of cortical bone but not at sites comprised of trabecular bone. All studies using estrogen treatment as a companion protocol have shown that calcium supplementation is inferior to estrogen in slowing cortical bone loss and that estrogen prevents trabecular bone loss completely. Some of these studies were randomized (55, 97, 98, 109, 112), but only two were blinded (109, 112). In the study of Smith et al (112) 40% of the subjects were lost to follow-up.

The results of a study performed by Recker et al (98) reflect those of the others. After two years, a supplement of 1.04 grams of elemental calcium, given as the carbonate salt, to 22 women between 55 and 65 years of age resulted in a 0.22% decrease in metacarpal cortical bone area as compared with a 1.18% decrease in 20 placebo-treated age-matched women ($p < 0.05$). By contrast, there was no difference in bone mineral content of the distal radius (mixture of trabecular and cortical bone). The effect of calcium supplementation to prevent metacarpal cortical bone loss was less than the effect of estrogen treatment in 18 age-matched women, and estrogen completely prevented bone loss at the distal radius. In a similar but nonrandomized study, Horsman et al (45) administered 800 mg of elemental calcium as the gluconate salt to 24 postmenopausal women over a two-year period and found a significant decrease in bone loss from the ulna (cortical bone) as compared to 18 placebo-treated control subjects. However, calcium treatment caused little if any diminution of the bone loss observed at the distal radius or in metacarpal cortices. Similarly, Nilas et al (79) found no change in bone

mineral content at the distal radius when three groups of women with calcium intakes varying from below 550 mg/day to greater than 1150 mg/day were administered a 500 mg elemental calcium supplement daily. However, an investigation performed by the same group (109) which was both randomized and blinded, found that the administration of 2000 mg/day of elemental calcium as the carbonate salt for two years to postmenopausal women slowed bone loss at the proximal forearm and slowed calcium loss from the total skeleton, while the loss of bone from sites composed predominantly of trabecular bone was no different from that of placebo-treated control subjects. As in previous studies, bone mineral content remained constant at all measurement sites in subjects receiving estrogen. In a nonrandomized study, Ettinger et al (24) found no effect of calcium supplementation up to 1500 mg/day, as the carbonate salt, on bone mineral content in the spine as assessed by QCT, or on distal radius or metacarpal cortical bone mass in 44 postmenopausal women as compared with 25 age-matched women who elected not to receive treatment. By contrast, 15 women who elected to take low-dose conjugated estrogen (0.3 mg/day) combined with 1500 mg of calcium per day demonstrated complete protection againts bone loss. This study and that of Cann et al (9) suggest the possibility that dietary calcium may play a permissive role in the maintenance of bone mass that is sex hormone dependent. However, Riis et al (108) found no potentiation of estrogen treatment by calcium supplementation.

Riggs et al (102) showed that the increased bone resorption surfaces observed in iliac crest bone biopsies from osteoporotic patients are restored toward normal by combined calcium and vitamin D supplementation. This effect was associated with a decrease in serum immunoreactive parathyroid hormone (iPTH) within the normal range, an event the authors justifiably speculated was responsible for the decrease in resorption surfaces. In a two-year randomized trial, severely osteoporotic women given 1200 mg/day of calcium had improved bone mineralization rates, compared to placebo-treated patients (87). The results of several other investigations, not involving bone histomorphometry, are consistent with this apparent antiresorption effect of calcium supplementation. Recker et al (98) showed that bone resorption was decreased when postmenopausal women were given supplements of calcium carbonate. Oral calcium suppresses hydroxyproline excretion, a well-established index of bone resorption, in osteoporotic postmenopausal women (44), but only under conditions of normal calcium absorption (77).

The evidence relating calcium supplementation to fracture prevalence is scanty. The only study of substance comes from the Mayo Clinic (105), reporting a nonrandomized but prospective assessment of the effect of various treatments of patients with generalized osteopenia on the occurrence of future vertebral fractures. In the study, 8 individuals received calcium carbonate

(1500–2500 mg/day) and 19 received calcium plus vitamin D (50,000 units once or twice a week). Both groups had 50% fewer vertebral fractures than did 27 placebo-treated and 18 untreated patients.

Recommendations and safety Calcium supplementation should not be used as a substitute for sex hormone replacement, which prevents postmenopausal bone loss in most patients (55, 97, 98, 109, 112) and appears to restore intestinal calcium absorption toward normal (27). There is little justification for providing women taking estrogen replacement more dietary calcium than the RDA. It would seem prudent to advise menopausal women who are unable (for medical reasons) or who refuse to take estrogen to consume at least 1000 to 1500 mg/day of calcium in their diets with the idea that supplementation above the RDA might help prevent loss of cortical bone and the development of chronic secondary hyperparathyroidism. Similarly, elderly men (> age 60 to 65 years) could benefit from supplementation for the same reasons.

Calcium treatment is safe in the absence of conditions that cause hypercalcemia or nephrolithiasis (40). Elemental calcium intakes in excess of 3000 to 4000 mg/day should be avoided because they will cause hypercalcemia in most subjects (47).

PHOSPHORUS Increased dietary phosphorus promotes fecal calcium loss but decreases urinary calcium excretion, thus maintaining calcium balance in most normal subjects on a high phosphorus diet (38, 116). The mechanism whereby increased dietary phosphorus decreases intestinal absorption of calcium has been investigated by Portale et al (94). They showed that increasing dietary phosphorus from <500 mg/day to 3000 mg/day decreased the production rate of $1,25(OH)_2D_3$ by the kidney. This observation strongly suggests that the ability to adapt to decreases or increases in dietary phosphorus depends upon the ability of the kidney to respond appropriately by increasing or decreasing $1,25(OH)_2D_3$ production.

The question arises, therefore, whether increases in dietary phosphorus might have an adverse influence on calcium economy in individuals whose kidneys have a limited capacity to produce 1,25(OH)2D3 or in those who need to be in positive calcium balance. Portale et al (93) reported that normal dietary phosphorus levels were sufficient to suppress plasma concentrations of $1,25(OH)_2D_3$ in children with moderate renal insufficiency. No studies of the influence of dietary phosphorus on calcium and bone metabolism have been reported in other populations that may be unduly sensitive to increments in dietary phosphorous above the RDA even though concern has been expressed (5, 61) that high phosphorus intakes may contribute to age-related bone loss in humans. On the other hand, chronic use of phosphate-binding antacids can

cause phosphate depletion and skeletal demineralization (115, 117). Since antacid use is common in North America, it should be considered an important risk factor in age-related bone loss, especially in those individuals who are calcium deficient (115).

VITAMIN D Prolonged and severe deficiency of vitamin D results in osteomalacia, a disorder characterized by an increased proportion of bone matrix that is not mineralized (91). Numerous studies over the past two decades suggest that elderly persons in the United States, Israel, Great Britain, and Europe are at increased risk for developing vitamin D deficiency. The most recent studies (15, 21, 86, 88, 122) report a progressive decline with aging in serum concentrations of the major circulating form of vitamin D, 25 hydroxyvitamin D (25OHD), but little convincing evidence is presented that the incidence of osteomalacia is increased in the elderly. It is speculated that these decreased serum levels of 25OHD are due to the tendency for older persons to have less exposure to the sun (95). MacLaughlin & Holick (63) have provided data supporting an alternative and possibly complementary explanation. They found an age-dependent decrease in epidermal concentrations of 7-dehydrocholesterol (provitamin D3) and that skin biopsies from elderly subjects had as much as a twofold lower capacity to produce vitamin D3 than biopsies from young adults. It is likely, therefore, that the elderly have a decreased capacity to biosynthesize vitamin D in the skin. Gallagher et al (29) reported that a three year trial of calcitriol in osteoporotic women caused improved calcium absorption and balance and decreased urinary hydroxyproline excretion. There were also preliminary indications of a decreased rate of vertebral fractures.

PROTEIN Few epidemiologic investigations bear on the issue of whether dietary protein influences calcium economy sufficiently to be a risk factor in osteoporosis. Marsh et al (69) reported more rapid postmenopausal cortical bone loss in omnivorous compared with vegetarian women, but protein intakes and sources were not analyzed for their potential contribution to this outcome measurement. It is also possible that lifestyle differences existed between the cohorts examined that may have confounded interpretation of the results. To circumvent this latter problem, the same investigators (68) evaluated cortical bone density in adult vegetarians, using their omnivorous mates as controls; the results tended to confirm those of the previous study.

Mazess & Mather (72) reported that the bone mineral content of a group of North Alaskan Eskimos was 10% to 15% lower than values for age-matched Caucasians and that the Eskimos had a high prevalence of osteoporotic vertebral fractures. The Eskimo diet contains approximately 200–400 g of protein/day, two to four times more than in the diets of non-Eskimo Amer-

icans; and the Ekimo diet is high in calcium and phosphorus. Clearly, dietary and lifestyle differences inherent in the Eskimo culture, and imposed by life in frigid climates with decreased exposure to ultraviolet light, could be as important or more important than protein intake in producing the bone mass changes observed in this study.

It is well established that *purified* protein, taken in increased quantities as an isolated nutrient, dramatically increases the renal excretion of calcium (41, 42). However, protein is not usually ingested as an isolated and purified nutrient; natural sources contain a myriad of other nutrients that could aggravate or counteract the calciuric effect of protein, per se. In 170 metabolic studies of perimenopausal women, Heaney & Recker (38) found that a 50% increase in protein intake from *natural whole foods* had a much smaller calciuric effect than that produced by purified proteins. These investigators calculated that a 50% increase in natural protein intake would lead to a negative calcium balance of −32 mg/day, an amount that approaches the −40 mg/day negative balance needed to account for the mean 1% to 1.5% loss in skeletal mass per year observed in postmenopausal women. It is thus possible that increases in dietary protein in perimenopausal women above approximately 55 grams/day could contribute significantly to the negative calcium balance frequently observed in this group. Many American perimenopausal women ingest diets containing considerably more protein than this (12). The effects of high protein diets in the elderly have not been systematically studied.

FIBER Studies over the past five decades (74, 99) have established that fiber chelates calcium (and other minerals) in the gastrointestinal tract, suggesting a potential cause of mineral deficiency. This process may increase osteoporosis risk in cultures such as in Iran where Bazari bread comprises as much as 50% of the caloric needs of children. This bread contains more calcium than white bread, but its high fiber and phytate content results in decreased intestinal absorption of calcium, magnesium, zinc, and phosphorus (99). However, the effect of fiber on mineral status at the levels consumed in the United States is unclear.

Kelsey et al (51) investigated the effects of 26 days of feeding a high fiber diet containing fruit and vegetables or a low fiber diet containing fruit and vegetable juice on calcium balance in 12 adult males. Balance was +72mg/day with the low fiber diet and −122 mg/day on the high fiber diet. In a follow-up study in which oxalate was removed from the diet, these investigators found that calcium balance was positive and was not influenced by fiber. Sandstead et al (110) found that fiber added to diets caused negative calcium balance, and they calculated that the requirement for calcium in the diet is increased as much as 150 mg/day when dietary fiber is increased by 26

grams. Cummings et al (13) showed that the addition of 31 grams of wheat fiber to the diets of subjects already taking a high protein diet produced a greater negative balance than high protein alone, suggesting an interaction of protein and fiber.

FLUORIDE Mertz (75) has argued that fluorine is an essential trace element which is responsible for growth and maintenance of bones and teeth. However, it seems unlikely that it plays a significant role in osteoporosis risk in the majority of Americans. Usual dietary fluoride intake is only 0.3 to 0.5 mg/d (48), and there appears to be no demonstrable effect on bone structure of an additional 1 to 2 mg/d of this ion as provided in fluoridated drinking water (1 ppm) (100).

By contrast, the incidence of osteosclerosis is high in areas where the fluoride concentration in drinking water is moderately high (5 to 10 ppm) (58). Leone (57) and Bernstein et al (6) have reported a lower prevalence of osteoporosis in these areas than in "low fluoride" regions. In areas with even higher fluoride intakes, such as the Punjab in India, crippling fluorosis occurs, but asymptomatic osteosclerosis is much more common (111).

In a prospective but nonrandomized study, Riggs et al (105) reported that treatment of osteoporotic patients with pharmacologic doses of fluoride and calcium reduced the vertebral fracture rate to approximately one quarter of untreated patients and to a significantly lower number than in patients treated with calcium alone. However, recent studies by two groups (53, 101) with a randomized, placebo-controlled and double blind design showed that although trabecular bone mineral density was increased in the group given fluoride (all subjects received calcium carbonate and a moderate physical exercise program) there was no difference in vertebral fracture rate from the group given placebo. Additionally, cortical bone mineral density was decreased and the rate of nonvertebral fractures increased in the fluoride-treated group. These results suggest that an inferior quality of bone is formed in the presence of fluoride despite cotreatment with calcium.

ALCOHOL Bone formation is decreased in patients who abuse alcohol. This causes a dramatic decrease in bone mass compared with normal subjects (7, 80). Since the risk of falling is increased in alcoholics, these two factors are probably responsible for the increased risk of hip fracture in alcoholic men and women and of vetebral fractures in alcoholic men.

Animal Studies

Nordin (81) has reviewed an extensive literature describing the many species that develop decreased bone mass as a result of calcium deficiency. In all of these studies, it is clear that the bone disease produced by calcium deficiency

most resembles osteoporosis. More recently, Jowsey & Gershon-Cohen (49) found that feeding adult cats a low calcium diet for five months decreased skeletal weight, decreased radiographic density of bone, and increased bone resorption. These changes were partially reversed by refeeding calcium. Presently, however, there is no completely satisfactory animal model of postmenopausal and/or age related osteoporosis, and this deficiency comprises a major impediment to future progress in osteoporosis research.

In contrast to the apparent inability of rather dramatic changes in dietary phorphorus to influence calcium balance in normal human subjects, there is considerable evidence in animals that diets containing relatively larger quantities of phosphorus than of calcium can cause hyperparathyroidism and bone loss (18). Almost all of these reports concern growing or aged animals and thus differ from investigations in humans (5), which in general focus on young or middle-aged adults.

ASSOCIATION OF NONDIETARY FACTORS WITH OSTEOPOROSIS

It is important for the reader to be aware that inadequate calcium nutriture per se is only a modest risk factor for osteoporosis. Other, nondietary factors are much more strongly associated with the disease. Risk and protective factors and their relative strengths are presented in Table 1. Several recent review articles discuss these important factors (23, 37, 60, 96).

Physical Activity

Immobilization can decrease bone mass (19, 20, 124). The osteoporosis produced can be localized (associated with fracture casting or painful limbs), generalized (associated with prolonged bed rest or space travel), or neurological (associated with paraplegia or quadriplegia). Its causes are unknown, but the absence of stress and muscle pull on bone may be a common etiologic factor. Resumption of normal weight-bearing activity restores both trabecular and cortical bone (73, 123).

The results of studies of the influence of increased physical activity on bone mass are mixed. Many studies have shown that exercise of sufficient intensity and duration as to produce amenorrhea can result in marked decreases in bone mineral density (10, 22, 59, 66, 78). However, among women who have amnorrhea from diverse causes, those who exercise regularly have greater bone density than those who are more sedentary (107).

Definite evidence is not available that regular exercise helps build peak bone mass in youth or retard bone loss in middle and old age (8). Most controlled trials have reported that moderate exercise may have a modest effect on preventing postmenopausal bone loss (2, 54, 125). Unfortunately,

Table 1 Risk and protective factors for the development of osteoporosis and fracture

Established		Suspected but not established
High	Intermediate	
Risk Factors		
Female sex	Low calcium diet	Family HX osteoporosis
Ovariectomy[a]	Early menopause	Caffeine intake
Advanced age	Thyroid Rx[b]	Alcohol, in moderation
White race	Antacids[d]	High protein diet
Thinness	Vitamin D deficiency	High fiber diet
Alcoholism	Hyperparathyroidism	Sedentary lifestyle
Steroid Rx[b]	Type I diabetes	
Disabling R. A.[c]	Cigarette smoking	
Tendency to fall		
Previous hip fracture		
Protective Factors		
Estrogens, long term use	Obesity	High calcium diet
Black race	High parity	Physical exercise
		Thiazide use

[a] Bilateral ovariectomy
[b] Chronic glucocortcoid or thyroid hormone administration in pharmacologic doses
[c] Rheumatoid arthritis
[d] Phosphate binding antacids taken in excess

none of these latter studies used a randomized design, and sample size and statistical power was inadequate in most. The effectiveness of walking in preventing bone loss has not been well studied. Nonetheless, since moderate exercise positively affects most health conditions, it would seem prudent to advise regular exercise throughout life.

SUMMARY

Calcium requirements may vary throughout the lifespan. During the growth years and up to age 25–30, it is important to maximize dietary intake of calcium to maintain positive calcium balance and achieve peak bone mass, thereby possibly decreasing the risk of fracture when bone is subsequently lost. The RDA for age 10–25 is 1200 mg/day. Calcium intake need not be greater than 800 mg/day during the relatively short period of time between the end of bone building and the onset of bone loss (30 to 40 years old). Starting at age 40–45, both men and women lose bone slowly, but women lose bone more rapidly around the menopause and for about 10 years after. Intestinal calcium absorption and the ability to adapt to low calcium diets are impaired in many postmenopausal women and elderly persons owing to a suspected

functional or absolute decrease in the ability of the kidney to produce $1,25(OH)_2D_3$. The bones then become more and more a source of calcium to maintain critical extracellular fluid calcium levels. Available evidence suggests that the impairments of intestinal calcium absorption observed during the menopause and aging can be overcome only by inordinately large calcium intakes (1500 to 2500 mg/day). Since this amount is difficult to derive from the diet, can cause constipation, and may not prevent trabecular bone loss, it should not be used as a substitute for sex hormone replacement. Women taking estrogen replacement should be provided the RDA for calcium of 800 mg/day at a minimum. Those who cannot or will not take estrogen should be asked to ingest at least 1000 to 1500 mg/day of calcium to delay cortical bone loss and prevent secondary hyperparathyroidism. It should be emphasized that up to 2000 mg/day of calcium is safe in teenaged children and adults.

Excessive dietary intake of protein and fiber may induce significant negative calcium balance and thus increase dietary calcium requirements. It is also possible that excessive intakes of phosphate could have a deleterious effect on calcium balance in populations whose need for calcium is great (e.g. growing children) or whose ability to produce $1,25(OH)_2D_3$ is impaired (e.g. the elderly). Moderation in the intake of these nutrients is urged.

Generally, the strongest risk factors for osteoporosis are uncontrollable (e.g. sex, age, and race) or less controllable (e.g. disease and medications). However, several factors such as diet, physical activity, cigarette smoking, and alcohol use are lifestyle related and can be modified to help reduce the risk of osteoporosis.

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